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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/017,084	10/24/2001	Avi J. Ashkenazi	GNE.2630P1C66	4358

35489 7590 01/13/2005

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EXAMINER

BLANCHARD, DAVID J

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicant No.

10/017,084

Applicant(s)

ASHKENAZI ET AL.

Examiner

David J Blanchard

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11/8/2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 59-65, 68-70 and 74-85 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 59-65 and 74-85 is/are rejected.
- 7) ☒ Claim(s) 68-70 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 October 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: Exhibits A & B.

DETAILED ACTION

1. Claims 1-58, 66-67 and 71-73 have been canceled.
Claims 59-65, 68-69 and 76 have been amended.
Claims 78-85 have been added.
2. Claims 59-65, 68-70 and 74-85 are pending and under examination.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
4. This Office Action contains New Grounds of Rejections.

Objections/Rejections Withdrawn

5. The rejection of claim 76 under 35 U.S.C 101 as being drawn to non-statutory subject matter is withdrawn in view of the amendment to the claim.
6. The rejections of claims 58 and 71-73, part a, under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the cancellation of the claims.
7. The rejection of claims 58 and 74-77 under 35 U.S.C. 102(b) as being anticipated by Struyk et al is withdrawn in view of Applicant's arguments and the amendments to the claims.

Response to Arguments

8. The rejection of claims 59-62 and 74 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained.

With respect to part a under item no. 16 of the previous Office Action (mailed 6/10/2004), the response filed 11/8/2004 has been carefully considered, but is deemed not to be persuasive. The response argues that the claims have been amended to recite an isolated nucleic acid encoding a polypeptide having at least 85-99% identity to the amino acid sequence of (a) or (b) or (c) or (d) or (e) and therefore, the phrase "wherein the nucleic acid encodes a polypeptide that is a mitogen for inner ear supporting cells" clearly refers to the isolated nucleic acids having at least 85-99% identity wherein these nucleic acids encode polypeptides that are mitogens for inner ear supporting cells. In response to this argument, it is pointed out that parts (c), (d) and (e) of claims 59-62 are drawn to nucleic acids and not amino acid sequences. Thus, as parts (c), (d) and (e) of claims 59-62 are drawn to the nucleic acid sequence of SEQ ID NO:522 or the full-length coding sequence of SEQ ID NO:522 and the preamble of the claims are drawn to variant nucleic acid sequences and fragments encoding variant polypeptides (i.e., 85-99% identity to SEQ ID NO:523). It remains unclear which of these nucleic acid sequences the phrase "wherein the nucleic acid encodes a polypeptide that is a mitogen for inner ear supporting cells" refers to.

With respect to part b under item no 16 of the previous Office Action (mailed 6/10/2004) the response filed 11/8/2004 did not address the lack of antecedent basis for

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the limitation "the nucleic acid" and as discussed above it remains unclear which nucleic acid the phrase refers to and part (e) of the claims does not recite any "nucleic acid".

New Grounds of Objections/Rejections

9. Claims 59-62 are objected to as being dependent upon a cancelled claim.

Appropriate correction is required.

10. Claims 59-65 and 74-77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite for reciting "The isolated nucleic acid of Claim 58 encoding a polypeptide having at least 85-99% sequence identity to:" in claims 59-62. Parts (c), (d) and (e) of the claims are drawn to nucleic acid sequences and not polypeptide sequences, thus, the claims are drawn to a polypeptide having at least 85-99% identity to the nucleic acid sequences of parts (c), (d) and (e). Are the claims drawn to nucleic acid sequences having 85-99% identity with the nucleic acid sequences of parts (c), (d) and (e) or are the claims drawn to nucleic acids which encode polypeptides having 85-99% identity with the amino acid sequences encoded by the nucleic acids of parts (c), (d) and (e) of the claims? Further, claims 63-65 are indefinite for reciting "An isolated nucleic acid comprising:" the nucleic acid of parts (c), (d) and (e) (see claim 63) and for reciting "The isolated nucleic acid of Claim 63 comprising the amino acid sequence". It is unclear what is contemplated by the

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phrases as nucleic acids may encode amino acid sequences, but do not comprise amino acid sequences.

Priority

The Examiner acknowledges and agrees with applicant's assessment that patentable utility for the subject matter defined in claims 59-65, 68-70 and 74-77 is based on the proliferation of rat utricular supporting cells assay (Example 116 at page 277 of WO 99/46281), which was first disclosed in PCT/US99/05028 (WO 99/46281), filed 3/8/1999 and patentable utility for the subject matter defined in claims 74-85 is based on the chondrocyte re-differentiation assay (Example 126 at page 359) and the glucose/FFA uptake assay (Example 117 at pages 355-356 of WO 00/53756) first disclosed in PCT/US00/04341 (WO 00/53756), filed 2/18/2000. Therefore, claims 59-65, 68-70 and 74-77 are granted the priority to 3/8/1999 and claims 74-85 are granted priority to 2/18/2000.

11. Claims 59-61, 74-80 and 82-84 are rejected under 35 U.S.C. 102(b) as being anticipated by Struyk et al (The Journal of Neuroscience, 15(3):2141-2156, March 1995) as evidenced by Gil et al (Journal of Neurobiology, 51:190-204, 2002).

The claims are interpreted as being drawn to isolated nucleic acids encoding a polypeptide having 85-95% identity to the amino acid sequence of SEQ ID NO:523, optionally lacking its associated signal peptide, wherein the encoded polypeptide is a mitogen for inner ear supporting cells, induces chondrocyte re-differentiation and stimulates the uptake of glucose or FFA by adipocyte cells. The claims are also drawn

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to a vector comprising the nucleic acids and a host cell comprising said vector, wherein the host cell is a CHO cell, an E.coli or a yeast cell.

Struyk et al teach a polynucleotide sequence encoding a polypeptide having 97% identity with the amino acid sequence of the polypeptide of SEQ ID NO:523 lacking its associated signal peptide, the amino acid sequence of the polypeptide encoded by the full-length coding sequence of SEQ ID NO:522, and the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 209487 (see Figure 3 and the alignment attached to the back of this Office Action; Exhibit A). Struyk et al teach that the polynucleotide was isolated from a Stratgene P5 rat brain library and plasmid rescue was carried out by excision with R408 helper phage (see page 2142, right column). Thus, Struyk et al teach a vector/plasmid comprising a polynucleotide encoding a polypeptide having 97% identity with the amino acid sequence of the polypeptide of SEQ ID NO:523 lacking its associated signal peptide, the amino acid sequence of the polypeptide encoded by the full-length coding sequence of SEQ ID NO:522, and the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 209487 as well as host cells comprising said vector/plasmid. Struyk et al also teach that the polynucleotide encodes a rat neurotrimin polypeptide having 97% identity with the polypeptide of SEQ ID NO:523, lacking its associated signal peptide (i.e., full-length coding sequence) (see Figure 3 and the sequence attached to the back of this Office action; residues 29-344 of SEQ ID NO:523) and neurotrimin is a member of the immunoglobulin gene superfamily (IgSF) of

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glycorylphosphatidylinositol (GPI) anchored cell adhesion molecules (see page 2141, right column and abstract). Further, Struyk et al teach that the cell adhesion molecules of the IgSF constitute a large family of proteins implicated in neural cell interactions and nerve fiber outgrowth during development (see bridging paragraph of pages 1214-1242. As evidenced by Gil et al (Journal of Neurobiology, 51:190-204, 2002) neurotrimin is a member of the IgLON family of GPI-anchored neural cell adhesion molecules (see abstract). As evidenced by the instant specification, the polynucleotide of SEQ ID NO:522, which encodes SEQ ID NO:523 (i.e., PRO337) is a newly identified member of the IgLON subfamily of the immunoglobulin superfamily and may possess neurite growth and differentiation potentiating properties (see page 179, lines 36-37).

Therefore, it is the Examiner's position that Struyk et al have produced a polynucleotide, which encodes a polypeptide that is a mitogen for inner ear supporting cells, induces chondrocyte re-differentiation and stimulates the uptake of glucose or FFA by adipocyte cells. One of ordinary skill in the art would reasonably conclude that the neurotrimin polypeptide of Struyk et al also possesses the same functional properties as those of the encoded polypeptides of SEQ ID NO:523 claimed and, therefore, it appears that Struyk et al has produced a polynucleotide that encodes a polypeptide that is functionally identical to the encoded polypeptide of SEQ ID NO:523 lacking its associated signal peptide. Since the Patent and Trademark Office does not have the facilities for examining and comparing the encoded polypeptide of SEQ ID NO:523 lacking its associated signal peptide claimed with the polypeptide of Struyk et al, the burden of proof is upon the Applicant to show a distinction between the functional

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characteristics of the claimed encoded polypeptide of SEQ ID NO:523 lacking its associated signal peptide and the encoded polypeptide of the prior art (Struyk et al). See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

13. Claims 74-85 are rejected under 35 U.S.C. 102(a) as being anticipated by Fukushima et al [a] (WO 99/58668, 11/18/1999) as evidenced by English equivalent Fukushima et al [b] (U.S. Patent 6,664,383 B1).

The claims are interpreted as being drawn to isolated nucleic acids encoding a polypeptide having 85-99% identity to the amino acid sequence of SEQ ID NO:523, optionally lacking its associated signal peptide, wherein the encoded polypeptide is induces chondrocyte re-differentiation and stimulates the uptake of glucose or FFA by adipocyte cells. The claims are also drawn to a vector comprising the nucleic acids and a host cell comprising said vector, wherein the host cell is a CHO cell, an E.coli or a yeast cell.

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Fukushima et al [a] teach an isolated nucleic acid encoding a polypeptide identical to the polypeptide of SEQ ID NO:523 (see SEQ ID NO:1 of Fukushima et al and the alignments attached to the back of this Office Action as Exhibit B). Fukushima et al teach a vector comprising the isolated nucleic acid and host cells comprising the vector, wherein the host cells are bacterial, yeast, insect or mammalian cells as evidenced by Fukushima et al [b] (see column 3 and SEQ ID Nos:1 and 2).

Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

Conclusions

14. No claim is allowed.

15. Claims 68-70 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.


16. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Respectfully,
David J. Blanchard
571-272-0827



LARRY R. HELMS, PH.D
PRIMARY EXAMINER

Exhibit A

QY	281	LEPHEPHASVALSGEGLHLEAGYVYGYVANYVTHDQVGLALASERANLYS	300
DB	1105	ATCTCTTCAATCTCTGACACAGTACAGGACATTCGCGACCTCCACAGAG	1166
QY	301	LEUGLYHLSHLEANALASERLEMEVLEPHAGIYPROGLVALVALSERGLVALSER	320
DB	1165	CTGGGCACACACCAATGCCAGGATCATCTATTATGTCACAGGCGCCGACACAGAGTGAC	1224
QY	331	AGAGLYTHSERHAGAGALGICVGLVALTPLEULNUPROTEULNULLEUHLISLEN	340
DB	1225	AAAGGACGTCAGAGAGGACAGGCTGGCTGTGCTCTGCTCTTCTTGATGTCACCTG	1286
QY	341	LEULEULYEPHE	344
DB	1285	CTTCTCAAAATTT	1296

RESULT 10					
RNT16845	RNT16845	2040 bp	mRNA	linear	ROD 26-MAY-1995
LOCUS	Rattus norvegicus neurotrophin mRNA, complete cds.				
DEFINITION					
ACCESSION	U16845				
VERSION	U16845.1 GI:755184				
KEYWORDS					
SOURCE	Rattus norvegicus (Norway rat)				
ORGANISM	Rattus norvegicus				

REFERENCE	1 (bases 1 to 2040)
AUTHORS	STRUYK, A. P., Canoll, P. D., Wolfgang, M. J., Rosen, C. L., D'Eustachio, P. and Salzer, J. L.
TITLE	Cloning of neurotactin defines a new subfamily of differentially expressed neural cell adhesion molecules
JOURNAL	J. Neurosci. 15 (3 Pt 2), 2141-2156 (1995)
MEDLINE	95198094
PubMed	7891157
REFERENCES	2 (bases 1 to 2040)
AUTHORS	Salzer, J. L.
TITLE	Direct Submission
JOURNAL	Submitted (02-NOV-1994) James L. Salzer, Cell Biology, NYU Medical Center, 550 First Avenue, New York, NY 10016, USA
FEATURES	location/Qualifiers
source	1. 2040
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	/accession="S09496-Dawley"
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 GNPPEVWTRHISPKRVAIGVSGDEBETLILQGLTRSGSDEKASNDVALPVRVNVV
 VNPVPSIAKGATGVPGVQKGLQCAASVPSAFQPKDQKDLVGGKGVVVRNP
 LSLTLTFPVSMDYGNVTCVASNRKQHTMAISIMDFGCAVSEVANGTSRRACIWLLE
 LMLTHLLKLP*

Alignment Scores:
 Pred. No.: 4,73e-95 Length: 2040
 Score: 2303.70 Matches: 326
 Percent Similarity: 71.22% Conservative: 13
 Best Local Similarity: 68.49% Mismatches: 4
 Query Match: 95.67% Indels: 133
 DB: 10 Gaps: 19

US-10-017-084A-523 (1-344) x RNT16645 (1-2040)

```
QY 1 Met-----Lys-----Thr-----IleGln-----ProLysMet----- 8
Db 91 TTGGATACCAAGTCTCTTAACTCTGTCCTAAAGTCCATGCTGAACTGCTACGCGGAGA 150
QY 9 -----His----- 9
Db 151 GCGAGCTCTGAGACCCCACTCTGCGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 210
QY 10 -----AsnSer----- 11
Db 211 GCGACCTTCTGCGCAAGCGACGACGAGAAAGTCCGCTGAGTGTGTGAACATG 270
QY 12 Ile-----SerTrp----- 14
Db 271 GTTCTCAGAGCTGCGACCTGAGCTGAGATTAGAGGAGAAATATTACCTTGACAGAGT 310
QY 15 -----AlaIlePhe-----Thr-----Gly 19
Db 331 CTGCGCGCT-----TTTCTCTCCAGAGCATGCGCGCGCTGAGTCAATCGCTGCTG 387
QY 20 -----LeuAla-----Ala----- 22
Db 388 CCGCGCGCTCACTCCCAACCCCACTTCTGCTGCTGCGCGCGCGCGCTGCTGCTGCTG 447
QY 23 -----Leu-----Cys-----LeuPhe 26
Db 448 CACTACCGGAGTTCTGGAGATTGTGCTGTGCGAGAAATGCGAGGCTGTGCGGATCTGTC 507
QY 27 -----Gln-----Gly 28
Db 508 CTGCGCTGGAAGTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 567
QY 29 ValProValArgSerGlyAspAlaThrPheProLysAlaMetAspAsnValThrValArg 48
Db 568 GTGCGCGCTGCTGAGGAGATGCGCACTTCCCAAGCTATGAGACACCTGACCGCTGAG 627
QY 49 GlnGlyGlnSerAlaThrLeuArgCysThrIleAspAsnArgValThrValAlaIleTrp 68
Db 628 CAGGCGGAGAGCGCCCACTCAAGTGCATTTGACACCGAGTCACTCCGAGTGGCTGCG 687
QY 63 LeuAsnArgSerThrIleLeuTyralGlyAsnAspLysTrpCysLeuAspProLysVal 88
Db 688 CTAAACCGGATGACATCTCTATGCTGAGAAATGACAAAGTGTGCTGATCTGCTGCTG 747
QY 89 ValLeuLeuSerAsnThrGlnThrGlnTyrSerIleGlnIleGlnAsnValAspValTyr 108
Db 748 GTTCTCTGAGTAAACCAACCAACCAACCAACCAACCAACCAACCAACCAACCAACCAAC 807
QY 109 AspGlnGlyProGlyThrCysSerValGlnThrAspAsnHisProLysThrSerArgVal 128
Db 808 GATTAGGCGCTTAACTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 867
QY 129 HisLeuIleValGlnValSerProLysIleValGlnIleSerSerAspIleSerIleAsn 148
Db 868 CACCTCACTTCTCAAGTATCTCCCAAAATGTGAGATTTCTTCAGATATCTCCATTAAT 927
QY 149 GlnGlyAsnAsnIleSerLeuThrCysIleAlaThrGlyArgProGlnProThrValThr 168
Db 928 GAAAGGAGACATCATGCTCATCTGATAGCCAGGTAGACCGAGCTACAGTAAAC 987
QY 169 TrpArgHisIleSerProLysValValGlyPheValSerGlnAspGlnTyrLeuGlnIle 188
Db 988 TGGAGCATATTTCTCCAAAGCTGTGCGCTTGTGTAGTAGAGTGAAGTCACTGAGATC 1047
QY 189 GlnGlyIleThrArgGlnGlnSerGlyAspTyrGlnCysSerAlaSerAsnAspValAla 208
Db 1048 CAGGCGATCACTCGGAGACACTCAGCGGAGATGAGTGCAGCGCTCCACGACGTGGCA 1107
QY 209 AlaProValValArgArgValValValThrValAsnTyrProProGlyIleSerGlnAla 228
Db 1108 GCAACGATGCTACAGAGATGACATCACTGATACATTCACATCAATCTCAAGACT 1167
QY 229 LysGlyThrGlyValProValGlyGlnLysGlyThrLeuGlnCysGlnAlaSerAlaVal 248
Db 1168 AAGGATGACAGGTGTCCCGTGGGAGCAAGAGGAGACTCTGCAAGTGTGAAGCTCGGCAATC 1227
QY 249 ProSerAlaGlnPheGlnIleTyrTyrValAspAspLysArgLeuIleGlnGlyLysGly 268
Db 1228 CTTCAAGCAAGATTTCTAGTGTCTGAGTCAAGATGACAAAGATCTGTGAGAGAGAGAGA 1287
QY 269 ValLysValGlnAsnArgProPheLeuSerLysIlePhePheAsnValSerGlnHis 288
Db 1288 GTCAAGTGGAAACACACTTTCCTTCAAGACTACACTTTTCACAGTCTGAAACAC 1347
QY 289 AspTyrGlyAsnTyrThrCysValAlaSerAsnLysLeuGlnIleThrAsnAlaSerIle 308
Db 1348 GACTATGGGAACTACACATGTGTGATCCAAAGTTGGCCACCAATGCCAGCATC 1407
QY 309 MetLeuPheGlnProGlyValAlaValSerGlnValSerAsnGlyThrSerArgArgAlaGly 328
Db 1408 ATCTATTTGGCCAGTGTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 1467
QY 329 CysValTyrPheLeuProLeuLeuValLeuHisLeuLeuLeuLysPhe 344
Db 1468 TGCATTTGGCTCTCCCTCTTCTGCTTAAACCTGCTCTCAATTT 1515
```

ALIGNMENTS

Exhibit B
1 of 3

RESULT 1

US-09-700-397-1

Sequence 1, Application US/09700397

Patent No. 6664383

GENERAL INFORMATION:

APPLICANT: One Pharmaceutical Co., Ltd.

TITLE OF INVENTION: No. 6664383el Polypeptides, cDNA encoding the same, and use of

FILE REFERENCE: 061459

CURRENT APPLICATION NUMBER: US/09/700.397

PRIOR FILING DATE: 2001-01-05

PRIOR APPLICATION NUMBER: JP 10-131815

PRIOR FILING DATE: 1998-05-14

PRIOR APPLICATION NUMBER: PCT/JP99/02485

NUMBER OF SEQ ID NOS: 19

SOFTWARE: Patent version 3.0

SEQ ID NO 1

LENGTH: 1032

TYPE: DNA

ORGANISM: Homo sapiens

US-09-700-397-1

Alignment Scores:

Pred. No.:	9-886-47	Length:	1032
Score:	2408.00	Matches:	344
Percent Similarity:	100.00%	Conservative:	0
Best Local Similarity:	100.00%	Mismatches:	0
Query Match:	100.00%	Indels:	0
DB:	4	Gaps:	0

US-10-017-084A-523 (1-344) x US-09-700-397-1 (1-1032)

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QY 1 MetLysThrIleGlnProlyseMetHisAnSerIleSerThrAlaIlePheThrGlyLeu 20
DB 1 ATGAAACATCTCAGCCAAATGCAATCTTCTTGGGCAATCTTCACGGGGCTG 60
QY 21 AlAlaIleCysLeuPheGlnGlyValProValArgSerGlyValAlaIlePheProlys 40
DB 61 GCTGCTCTGTCTCTTCCACAGAGTCCCGTCGCGACGAGATGCACTTCCCAAA 120
QY 41 AlAmeCAsPheValThrValArgGlnGlyGlyIleSerAlaThrIleuArgCysThrIle 60
DB 121 GCTATGCAACAGTACGCTCCGCGAGGGAGAGAGCCCACTCAGAGGCACTTATAC 180
QY 61 AsnArgValThrArgValAlaIlePheLeuAnArgSerThrIleuArgAlaIleValAn 80
DB 181 AACCGGATCACCGGGGTGGCTGGCTTAAACCGACGACCACTCTATGCTGGAGATAC 240
QY 81 LysTrpCysLeuAnPProArgValValIleuSerAnThrGlnThrGlnIleSerIle 100
DB 241 AAGTGTGCTGCTGATCTCTGCTCTTCTTGAAGCAACCCAAAGCACTGACATC 300
QY 101 GlnIleGlnAnValAlaArgValIleArgGlnGlyProIleThrCysSerValGlnThr 120
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DB 301 GAGATCCAGAACGTAGATGTGTATGACGAGGGCCCTTACACCTGCTGGTCAGACAGAC 360
QY 121 AsnHisProlyseThrSerArgValIleGlnIleValGlnValSerProlyIleValGlu 140
DB 361 AACCAACCCAAAGACCTTACAGGTCACTCATGTGCAAGATCTTCCCAAAATGTGTAG 420
QY 141 ILeSerSerAapIleSerIleAnGlnGlyValAnAnIleSerLeuThrCysIleAlaThr 160
DB 421 ATTCTTCAGATATCTCATTAATGAGGAAACAATATTAGCTTCACTGCAATGCAACT 480
QY 161 GlyArgProGluProThrValThrTrpArgHisIleSerProlyValAlaGlyPheVal 180
DB 481 GGTAAACAGAGCTTACGGTACTTGAACACACTCTCCCAAGCGCTGGCTTGTG 540
QY 181 SerGluAnPProIleuGlnIleGlnGlyIleThrArgGlnIleSerGlyAspTrpGlu 200
DB 541 ACTGAAACAGCAATCTTGAATTCAGGCGATCACCCCGAGCACTGACGGGACTACGAG 600
QY 201 CysSerAlaSerAnPValAlaIleProValValArgValIleValThrValAn 220
DB 601 TCCAGTCTCTCAATGAGTGGCCGCGCGGTGACGAGATGAAAGTAAAGTCACTGAC 660
QY 221 TrpProProIleIleSerGluAlaValArgIleValThrGlyValProValGlyGlnIle 240
DB 661 TATCCACCATTCATTCAGAACCCAGGAGGTACAGGTGCTCCCGGACCAAAAGGGGACA 720
QY 241 LeuGlnCysGluAlaSerAlaValProSerAlaGluPheGlnIleTrpIleValAsp 260
DB 721 CTGCACTGTAAAGCTTACAGATCCCTTCAAGCAAAATTCAGGTGAAAGTAAAGTAA 780
QY 261 ArgLeuIleGlnGlyValIleValGlyValIleValGluAnArgProPheLeuSerIle 280
DB 781 AACTGATATTAAGAAAGAAAGGCGTAAAGTGAAGAAACCACTTCTCTCAAAATC 840
QY 281 IlePhePheAnValSerGluHisAapTrpGlyAnTrpIleThrCysValAlaSerAn 300
DB 841 ATCTTCTCAATGTCTTGAACATGACTATGAGCACTTCTGCTGCTCTCAACAG 900
QY 301 LeuGlyHisThrAnAlaSerIleuLeuPheGlyProGlyAlaValSerGluValSer 320
DB 901 CTGGCCACACCAATGCAAGCATGCTATTTGTTCAGGCGCGCTCACAGGTGAGC 960
QY 321 AsnGlyThrSerArgValArgIleCysValIlePheLeuProLeuValIleuHisIle 340
DB 961 AACGGCAGCTGAGAGAGGCGAGGCTGGCTGCTGCTCTTCTGCTTGGTCTTGAACCT 1020
QY 341 LeuLeuLysPhe 344
DB 1021 CTCTCAAAATTT 1032
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RESULT 2
US-09-700-397-2
Sequence 2, Application US/09700397
Patent No. 6664383
GENERAL INFORMATION:
APPLICANT: One Pharmaceutical Co., Ltd.
TITLE OF INVENTION: No. 6664383el Polypeptides, cDNA encoding the same, and use of
FILE REFERENCE: 061459
CURRENT APPLICATION NUMBER: US/09/700.397
PRIOR FILING DATE: 2001-01-05
PRIOR APPLICATION NUMBER: JP 10-131815
PRIOR FILING DATE: 1998-05-14
PRIOR APPLICATION NUMBER: PCT/JP99/02485
NUMBER OF SEQ ID NOS: 19
SOFTWARE: Patent version 3.0
SEQ ID NO 2
LENGTH: 1693
TYPE: DNA
ORGANISM: Homo sapiens
FEATURE:
NAME/KEY: misc feature
OTHER INFORMATION: Clone OC001 derived from human brain

Exhibit B
2 of 3

NAME/KEY: CDS
LOCATION: (130) .. (1161)
NAME/KEY: sig peptide
LOCATION: (130) .. (213)
NAME/KEY: mac peptide
LOCATION: (214) .. (1)
US-09-700-397-2

Alignment Scores:

Pred. No.: 8,186-46 Length: 1,693
Score: 2408.00 Matches: 344
Percent Similarity: 100.00 Conservative: 0
Best Local Similarity: 100.00 Mismatches: 0
Query Match: 100.00 Indels: 0
DB: 4 Gaps: 0

US-10-017-084a-523 (1-344) x US-09-700-397-2 (1-1693)

QY 1 Metlyethr11eg1nProlysmeth18amser11eser1p1allephethr1y1leu 20
DB 130 ATGAAACCATTCAGCCAAATGCAATTCATCTTGCGCATCTTCAGCGGCGCTG 189
QY 21 A1a1aleu1Cy1e1u1Phe1ng1y1Val1ProVal1ArgSer1y1Asp1a1Thr1Phe1Proly 40
DB 190 GCTGCTCTGCTCTCTTCAGAGAGTCCCGTCCGAGCGAGAGTCCCGCTTCCTCCCA 249
QY 41 A1a1a1e1a1Phe1nVal1Thr1Val1Arg1ng1y1G1u1Ser1a1Thr1Leu1Arg1y1e1a1P 60
DB 250 GCTATGACCAAGTGAAGTCCGCGAGGAGAGAGCGCACTTCAGTGCATTAATGAC 309
QY 61 Aa1a1a1Val1Thr1Arg1Val1a1a1Thr1Leu1a1a1Ser1Thr11e1u1y1A1a1A1a1P 80
DB 310 AACCGAGTCAACCGAGTGCCTGCTTAAACCGAGCACTTCCTTA1a1a1GCTGAGATAC 369
QY 81 Ly1e1TP1Cy1e1u1a1P1ro1a1y1Val1Leu1e1u1Ser1a1Thr1G1n1y1Ser11e 100
DB 370 AAGTGTCTGATCTCTGATCTCTGCTGCTCTCTGAGCAACCGCAACCGCATACGATC 429
QY 101 G1u11e1G1a1n1a1a1P1a1P1a1y1A1a1P1a1y1P1ro1y1Thr1Cy1Ser1y1A1a1Thr1a1P 120
DB 430 GAGATCTCAAGACGTGAGATGTATGACAGAGGCTTACCTGCTGCTGCTGACAGAC 489
QY 121 Aa1a1e1P1roly1e1r1Ser1a1y1A1a1e1u1e1Val1G1n1a1Ser1Proly1e1Val1G1u 140
DB 490 AACCAACCAAGACCTCTAGAGTCCACTCATTTGTGCAATCTTCCCAATTTGTAG 549
QY 141 11e1Ser1e1a1P1e1Ser11e1a1n1G1y1A1a1a1a1e1Ser1e1u1Thr1Cy11e1a1Thr 160
DB 550 ATTCTTCAATCTCTCAATCTCTTAATGAGAGCAATTAAGCTTCACTGATACATCACT 609
QY 161 G1y1a1g1P1ro1y1P1ro1Thr1Val1Thr1Thr1a1a11e1Ser1Proly1a1a1Val1G1y1Phe1a1 180
DB 610 GGTAGACCAAGCTTACGCTTACCTGAGACCACTCTTCCCAACCGGTGCTTGTG 669
QY 181 Ser1G1u1a1P1roly1e1r1Leu1G1u1e1G1n1y11e1Thr1Arg1G1u1n1Ser1y1a1P1y1G1u 200
DB 670 AGTGAAGACCAATCTGGAATTCAGAGGATCAACCGAGAGCGTCAAGGAGTACAG 729
QY 201 Cy1Ser1a1a1Ser1a1a1P1a1a1a1P1roVal1a1a1Arg1y1a1y1e1a1Thr1a1a1n 220
DB 730 TGCAGTCTCTCAAGTGAAGTCCCGCTGCTGAGAGATTAAGATCAACCGTAAAC 789
QY 221 Ty1P1ro1Proly1e1Ser1G1u1a1y1e1G1y1Thr1y1Val1ProVal1G1y1G1u1y1G1y1Thr 240
DB 790 TATTCACCAATCTTCAAGTGAAGCGTCAAGGATCAAGTGTCCCGTGAAGCAAAAGGAGCA 849
QY 241 Leu1G1n1Cy1e1G1u1a1Ser1a1a1P1roSer1a1a1u1Phe1a1Thr1y1Thr1a1a1P1y1s 260
DB 850 CTCAGATGTGAAGCTCTCAAGTCTCCCTCAAGCAATTCAGAGTGAAGATGAAGCAAA 909
QY 261 Arg1Leu11e1G1u1y1e1y1e1G1y1a1y1e1Val1G1u1a1a1P1roPhe1Leu1Ser1y1e1u 280
DB 910 AGCATATTTGAAGAAAGAGAGGCTGAGAGTGAAGAAAGCAAGACCTTCTCTCAAAATCTC 969

QY 281 11e1Phe1a1a1Val1Ser1G1u1a1a1P1ro1y1y1A1a1a1Thr1Cy1e1a1a1a1Ser1a1y1s 300
DB 370 ATTCTTCAATCTCTCAAGTGAAGTCCCGCTGAGATCACTTCCCGCTTCAAGAG 1029
QY 301 Leu1G1y1e1Thr1a1a1a1Ser11e1e1Leu1Phe1G1y1ProG1y1A1a1a1Ser1G1u1a1Ser 320
DB 1030 CTGGGCAACCAATGCCAGATCATCTTAATTTGCTCAAGCGCGCTGAGAGGCTGAGC 1089
QY 321 Aa1a1y1Thr1Ser1Arg1Arg1G1y1Cy1e1Val1Thr1Leu1e1P1ro1Leu1e1u1a1e1u1a1e1u 340
DB 1090 AACGCACTCTCAAGAGAGGAGGAGTGCCTGCTGCTGCTCTTGTGATCTTCAACTG 1149
QY 341 Leu1e1u1y1e1Phe 344
DB 1150 CTTCCAATTT 1161

RESULT 3 397-5
US-09-700-397-5 Application US/09700397

/ Sequence 1 Application US/09700397
/ Patent No. 6664383
/ GENERAL INFORMATION:
/ APPLICANT: Pro Pharmaceutical Co., Ltd.
/ TITLE OF INVENTION: No. 6664383el Polypeptides, cDNA encoding the same, and use of
/ FILE REFERENCE: 061459
/ CURRENT APPLICATION NUMBER: US/09/700 397
/ PRIOR FILING DATE: 2001-01-05
/ PRIOR FILING DATE: 1998-05-14
/ PRIOR APPLICATION NUMBER: PCT/JP99/02485
/ PRIOR FILING DATE: 1999-05-13
/ NUMBER OF SEQ ID NOS: 19
/ SOFTWARE: Patent version 3.0
/ SEQ ID NO 5
/ LENGTH: 939
/ TYPE: DNA
/ ORGANISM: Homo sapiens
US-09-700-397-5

Alignment Scores:

Pred. No.: 2,336-41 Length: 939
Score: 2185.00 Matches: 313
Percent Similarity: 100.00 Conservative: 0
Best Local Similarity: 100.00 Mismatches: 0
Query Match: 90.744 Indels: 0
DB: 4 Gaps: 0

US-10-017-084a-523 (1-344) x US-09-700-397-5 (1-939)

QY 32 Arg1e1r1y1e1P1a1a1Thr1Phe1Proly1a1a1e1a1Phe1nVal1Thr1Val1Arg1n1y1G1u 51
DB 1 CGACCGAGATTCACCTTCCCAAGCTTAAGCAACGTGAAGTCCCGAGGAGAG 60
QY 52 Ser1a1a1e1u1Arg1y1Thr11e1a1Phe1a1y1a1a1Thr1Arg1Val1a1a1P1ro1a1a1y1 71
DB 61 AGCGCTCTCTGAGTCACTATTAACAACCGAGTCCCGAGGAGGCTGCTTAAACCGC 120
QY 72 Ser1Thr1Leu1y1r1a1a1a1a1P1ro1y1e1r1P1y1e1a1P1ro1a1a1y1a1a1e1u1e1u 91
DB 121 AGCCATCTCTATCTGAGATTAAGTGTCTGATCTCTGATCTCTGATCTCTG 180
QY 92 Ser1a1a1Thr1G1n1y1Thr1Ser11e1G1u11e1G1n1a1n1a1P1roVal1y1Thr1a1g1G1u1y 111
DB 181 AGCAACCGCAACCGAGTCAAGATCAAGATCAAGAGTGAAGTGAAGAGAGGAGC 240
QY 112 Pro1y1Thr1Cy1Ser1Val1G1n1Thr1a1Phe1a1a1P1roly1e1r1Ser1a1y1a1e1u1e1 131
DB 249 CTTTACCTCTCTGAGTGAAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 300
QY 132 Val1G1n1a1e1P1roly1e1r1e1Val1G1u11e1Ser1e1a1P1e1Ser11e1a1n1G1y1a1n 151
DB 301 GTCAGATCTCTCCAAATTTGAAGATTTCTTCAGATCTCTCAATTAAGAGAGAG 360

ALIGNMENTS

Exhibit B
2 of 3RESULT 1
US-09-700-397-2

Sequence 2, Application US/09700397

Patent No. 6664383

GENERAL INFORMATION:

APPLICANT: Ono Pharmaceutical Co., Ltd.

TITLE OF INVENTION: No. 6664383el Polypeptides, cDNA encoding the same, and use of

FILE REFERENCE: 061459

CURRENT APPLICATION NUMBER: US/09/700,397

PRIOR FILING DATE: 1998-05-14

PRIOR APPLICATION NUMBER: PCT/JP99/02485

NUMBER OF SEQ ID NOS: 19

SOFTWARE: PatentIn version 3.0

SEQ ID NO 2

LENGTH: 1693

TYPE: DNA

ORGANISM: Homo sapiens

NAME/KEY: misc feature

OTHER INFORMATION: Clone OC001 derived from human brain

NAME/KEY: CDS

LOCATION: (130)..(1161)

NAME/KEY: sig peptide

LOCATION: (130)..(213)

NAME/KEY: mat peptide

LOCATION: (214)..()

US-09-700-397-2

Query Match

Best Local Similarity 100.0%; Score 1035; DB 4; Length 1693;

Matches 1035; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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QY 1 ATGAAACATTCAGCCAAATTCATCTCTGGGCAATCTTCAGCGGCTG 60
DB 130 ATGAAACATTCAGCCAAATTCATCTCTGGGCAATCTTCAGCGGCTG 189
QY 61 GCTGCTGTGTCTCTTCAGAGAGTCCGTCGAGCGAGATGCCATCTCCCAA 120
DB 190 GCTGCTGTGTCTCTTCAGAGAGTCCGTCGAGCGAGATGCCATCTCCCAA 249
QY 121 GCTATGACAGAGAGTCCGTCGAGCGAGAGAGAGAGAGAGAGAGAGAG 180
DB 250 GCTATGACAGAGAGTCCGTCGAGCGAGAGAGAGAGAGAGAGAGAGAG 309
QY 181 AACCGGTCACCGGTCGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 240
DB 310 AACCGGTCACCGGTCGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 369
QY 241 AAGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGT 300
DB 370 AAGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGT 429
QY 301 GAGATTCAGAGAGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGT 360
DB 430 GAGATTCAGAGAGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGT 489
QY 361 AACCAACCAACCAACCAACCAACCAACCAACCAACCAACCAACCAACCA 420
DB 490 AACCAACCAACCAACCAACCAACCAACCAACCAACCAACCAACCAACCA 549
QY 421 ATTCTTCAGATTCATTCATTCATTCATTCATTCATTCATTCATTCATTC 480
DB 550 ATTCTTCAGATTCATTCATTCATTCATTCATTCATTCATTCATTCATTC 609
QY 481 GGTAGACAGAGAGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGT 540
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DB 610 GGTAGACAGAGAGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGT 669
QY 541 AGTGAAGAGAGATTCATTCATTCATTCATTCATTCATTCATTCATTCATTC 600
DB 670 AGTGAAGAGAGATTCATTCATTCATTCATTCATTCATTCATTCATTCATTC 729
QY 601 TCGAGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGT 660
DB 730 TCGAGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGT 789
QY 661 TATCCACATTCATTCATTCATTCATTCATTCATTCATTCATTCATTCATTC 720
DB 790 TATCCACATTCATTCATTCATTCATTCATTCATTCATTCATTCATTCATTC 849
QY 721 CTGAGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGT 780
DB 850 CTGAGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGT 909
QY 781 AGACTGATTCAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 840
DB 910 AGACTGATTCAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 969
QY 841 ATCTTCTTCAATGTCTCTGAAATGAGATTCATTCATTCATTCATTCATTC 900
DB 970 ATCTTCTTCAATGTCTCTGAAATGAGATTCATTCATTCATTCATTCATTC 1029
QY 901 CTGGGCAACCAATTCAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 960
DB 1030 CTGGGCAACCAATTCAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 1089
QY 961 AACGCACTTCAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 1020
DB 1090 AACGCACTTCAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 1149
QY 1021 CTCTCAATTTTGA 1035
DB 1150 CTCTCAATTTTGA 1164
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RESULT 2

US-09-700-397-1

Sequence 1, Application US/09700397

Patent No. 6664383

GENERAL INFORMATION:

APPLICANT: Ono Pharmaceutical Co., Ltd.

TITLE OF INVENTION: No. 6664383el Polypeptides, cDNA encoding the same, and use of

FILE REFERENCE: 061459

CURRENT APPLICATION NUMBER: US/09/700,397

PRIOR FILING DATE: 1998-05-14

PRIOR APPLICATION NUMBER: PCT/JP99/02485

NUMBER OF SEQ ID NOS: 19

SOFTWARE: PatentIn version 3.0

SEQ ID NO 1

LENGTH: 1032

TYPE: DNA

ORGANISM: Homo sapiens

US-09-700-397-1

Query Match

Best Local Similarity 99.7%; Score 1032; DB 4; Length 1032;

Matches 1032; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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QY 1 ATGAAACATTCAGCCAAATTCATCTCTGGGCAATCTTCAGCGGCTG 60
DB 1 ATGAAACATTCAGCCAAATTCATCTCTGGGCAATCTTCAGCGGCTG 60
QY 61 GCTGCTGTGTCTCTTCAGAGAGTCCGTCGAGCGAGATGCCATCTCCCAA 120
DB 61 GCTGCTGTGTCTCTTCAGAGAGTCCGTCGAGCGAGATGCCATCTCCCAA 120
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